SHORT COMMUNICATION

The use of ^{131}I -MIBG in the imaging of metastatic carcinoid tumoursD.I. Jodrell¹, A.T. Irvine², V.R. McCready², E. Woodcraft² & I.E. Smith¹Departments of Medicine¹ and Nuclear Medicine², Royal Marsden Hospital, Fulham Road, London, SW3, UK.

Meta-iodobenzylguanidine (MIBG) is an analogue of nor-adrenalin which concentrates in adrenergic vesicles. Studies performed with an iodine-131 radiolabelled form (^{131}I -MIBG) have shown that it can be used as an imaging agent for the adrenal medulla (Fischer *et al.*, 1984) and its neoplasms (phaeochromocytoma and neuroblastoma) (Hoefnagel *et al.*, 1987; Kimmig *et al.*, 1984). ^{131}I -MIBG has also been shown to localise in paraganglioma, another tumour arising from the sympathetic nervous system (Pease & Polak, 1978), and in medullary carcinoma of the thyroid (Shapiro *et al.*, 1985). These tumours show a common APUD (amine precursor uptake and decarboxylation) mechanism (Sisson *et al.*, 1981). Carcinoid tumours also possess a number of APUD properties, including in particular neurosecretory (dense core) granules and the ability to produce a variety of biogenic amines. Preliminary studies have suggested that carcinoid tumours may also take up ^{131}I -MIBG (Sisson *et al.*, 1984; Smit *et al.*, 1984).

If carcinoid tumours were shown to take up this radio-pharmaceutical with sufficient concentration then it might be possible to achieve therapeutic doses of ^{131}I -MIBG, a technique successfully employed with malignant phaeochromocytoma (Sone *et al.*, 1985).

We describe a study to investigate further the uptake of ^{131}I -MIBG for diagnostic imaging in 11 patients with confirmed metastatic carcinoid tumours.

Eleven patients known to have metastatic carcinoid tumours were studied. In 5 patients secondary deposits were histologically confirmed as carcinoid. The remaining 6 patients had metastatic tumours diagnosed by CT scanning or ultrasound and elevated urinary 5 hydroxyindoleacetic acid (SHIAA) levels, the original primary tumour had been diagnosed histologically. Ten of the 11 patients had abdominal CT scan or ultrasound to document metastases. An NMR scan was performed in one patient (10). Bone scans were only performed in patients with bone pain. Patient details are shown in Table I.

The patients received 0.3 ml of Lugol's iodine 3 times a day for 3 days prior to and 3 days after administration of ^{131}I -MIBG to prevent thyroid uptake of the radioiodine.

^{131}I -MIBG (20-40 mBq) was injected intravenously. Imaging was performed at 24 and 48 h following injection for all patients, and at 72 h in 6 patients, using a Siemen's ZLC75 Gamma camera.

A medium energy collimator was used with the peak set at 350 KeV and a window of 15%. Images were acquired over 600 seconds. Planar anterior and posterior views of the chest and abdomen were taken with selective views of clinically involved areas.

Table I Patient characteristics.

Age	41-72	(Median 60)
Sex	M: 5	F: 6
No. of sites of disease	1-3	(Median 1)
SHIAA levels	115-1,198	(Median 845) $\mu\text{mol } 24\text{ h}^{-1}$
Sites of primary tumour	Ileum 4, Ovary 1, Lung 2	Unknown 4

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Uptake at tumour sites was compared with normal uptake both in the liver and the myocardium.

The levels of ^{131}I -MIBG in the areas involved by carcinoid tumour in relation to the myocardial and liver uptakes are summarised in Table II together with the sites of disease, symptoms experienced and urinary SHIAA levels for individual patients.

In 8 (73%) patients unequivocal abnormal uptake was seen. One patient (8) had abnormal uptake in a single area within the liver, whereas CT scan showed multiple metastases. One patient (2) demonstrated a mixture of 'hot' and 'cold' areas in the liver. In 3 patients no abnormal uptake was seen. No sites of disease were identified on ^{131}I -MIBG scintigraphy that were not also detectable by other tests. One patient (5) with a negative ^{131}I -MIBG scintigram was the only patient in our group to have bone metastases (histologically proven) and he also suffered no 'carcinoid' symptoms. A $^{99\text{Tcm}}$ methylenediphosphonate bone scintigram showed multiple areas of increased uptake, and this appearance was shown to be gradually progressing over a 4-year period. A second patient with a negative ^{131}I -MIBG scintigram (11) had only moderately elevated SHIAA levels and was asymptomatic. The third had a lung primary with hepatic metastases, an elevated SHIAA and marked symptoms. The liver metastases were documented by ultrasound and CT scanning.

We found no correlation between the urinary SHIAA levels and ^{131}I -MIBG uptake in the tumours. One patient (6) had levels only modestly raised at $132\mu\text{mol } 24\text{ h}^{-1}$ ($N < 75\mu\text{mol } 24\text{ h}^{-1}$) but an unequivocally positive scintigram and marked symptoms while another patient with SHIAA levels 5 times this level had a negative scintigram.

We also found no relationship between 'carcinoid symptomatology' and ^{131}I -MIBG uptake. Patient 5 suffered florid carcinoid symptoms (with elevated urinary SHIAA levels) but no uptake of the ^{131}I -MIBG was seen.

We did not observe an increase in uptake of the ^{131}I -MIBG after 48 h and therefore scanning at 72 h was discontinued. Compared with other studies we saw low levels of myocardial activity at 48 h (none in 6/11 patients).

Our results confirm that ^{131}I -MIBG is preferentially taken up by the majority of metastatic carcinoid tumours, with a 73% positive uptake in this study compared with 63% in Hoefnagel's series (Hoefnagel *et al.*, 1987). However, this incidence is lower than in malignant phaeochromocytoma where more than 90% of lesions take up ^{131}I -MIBG (Wieland *et al.*, 1981). In keeping with other authors we found no correlation between urinary SHIAA and ^{131}I -MIBG uptake. However, we were unable to confirm the relationship between carcinoid symptomatology and ^{131}I -MIBG uptake reported by Hoefnagel *et al.* (1987).

We were unable to demonstrate preferential uptake of radiolabelled MIBG in particular sites. Although our only patient with bony metastases did not show any uptake of ^{131}I -MIBG, Hoefnagel found that 2 of 3 patients with bone involvement showed abnormal uptake.

In 2 patients the uptake varied from lesion to lesion. The ^{131}I -MIBG scintigram suggested a solitary hepatic metastasis, while the CT scan showed multiple lesions. It is possible that these appearances represent a mixture of func-

Table II

Patient	Urinary 5HIAA <i>N</i> < 75 $\mu\text{mol } 24 \text{ h}^{-1}$	Sites	'Carcinoid' symptoms	^{131}I -MIBG uptake	Myocardial uptake	Confirmatory tests
1	845	Li, P	D	Li = 3, P = 2	0	CT Histo
2	208	Li	D	Li = 3 and 0	0	CT
3	957	Li	D, F, B	Li = 3	1	US
4	986	Li	Nil	Li = 3	0	CT Histo
5	658	Li	D, F, B	No abnormal uptake	0	US Histo
6	132	Li	D, F, B	Li = 3	1	CT
7	115	B	Nil	No abnormal uptake	0	XR Bone scan
8	1,198	Li, S, N	D	Li = 3, S = 2, N = 0	0	CT US Histo
9	517	Li	F	Li = 3	1	US CT
10	871	Lu, M, N	D, F	Li = 3, M = 3 ^a	2	CT NMR Histo
11	177	Li, Lu	Nil	No abnormal uptake	1	CT Histo

^a*N* obscured by liver.

Sites: Li = Liver N = Nodes Symptoms: F = Flushing
Lu = Lung P = Pelvic mass D = Diarrhoea
B = Bone M = Mesentery B = Bronchospasm
S = Spleen

Uptake grade: 0 No activity
1 Less than normal liver
2 Similar to normal liver
3 Greater than normal liver

tioning and non-functioning lesions, or alternatively poorly functioning lesions may not be seen due to the low activities used and the limitations of planar imaging. This variability of uptake may have implications in future attempts at therapy.

The preferential uptake of ^{131}I -MIBG by pheochromocytomas has led to successful attempts at radiotherapeutic

ablation using larger doses of this radiopharmaceutical (Sone *et al.*, 1985). A small number of patients with carcinoid have also been treated in this way and although some symptomatic improvements have been seen, no tumour regression has so far been reported (Hoefnagel *et al.*, 1987). Nevertheless the frequency of positive uptake suggests that the therapeutic potential merits further investigation.

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